AR/1652

Docket No.: PF-0148-3 CPA

Response Under 37 C.F.R. 1.116 - Expedited Procedure

Examining Group 1652

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of: Hawkins et al.

Title: HUMAN PYROPHOSPHATASE

Serial No.: 09/415,540 Filing Date: October 08, 1999

Examiner: Slobodyansky, E. Group Art Unit: 1652

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FEE TRANSMITTAL SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Return Receipt Postcard;
2. Brief on Appeal, including Appendix (16 pp., in triplicate); and
3. Exhibit A (in triplicate).

The fee has been calculated as shown below.

Claims	Claims After Amendment		Claims Previously Paid For		Present Extra	Other Than Small Entity Rate	Fee		Additional Fee(s)
Total	3		20		0	x$18.00	0	$	0
Indept.	1		3		0	x$84.00	0	$	0
First Presentation of Multiple Dependent Claims						+280.00	0	$	0
Total Fee:								$	0

X Fee for filing a Brief in support of an Appeal under 37 CFR 1.17(c): $ 10.00

X Please charge Deposit Account No. **09-0108** in the amount of : $ 10.00

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 09-0108. **A duplicate copy of this sheet is enclosed.**

Respectfully submitted,
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Date: 6 May 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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Serial No.:	09/415,540	Filing Date:	October 08, 1999
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BRIEF ON APPEAL

Sir:

Further to the Notice of Appeal filed 28 February 2003, and received at the Patent Office on 06 March 2003, herewith are three copies of Appellants' Brief on Appeal. Authorized fees include the $10 fee for the filing of this Brief ($320 for the filing of the instant Brief under 37 C.F.R. § 1.17(c), minus a credit of the $310 fee for the filing of the Brief on Appeal of 26 November 2001, per M.P.E.P. § 1208.02).

This is an appeal from the decision of the Examiner rejecting claims 18-20 of the above-identified application.

(1) REAL PARTY IN INTEREST

The above-identified application is assigned of record Incyte Pharmaceuticals, Inc., (now Incyte Corporation, formerly known as Incyte Genomics, Inc.) (Reel 8437, Frame 0115) which is the

real party in interest herein.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

(3) STATUS OF THE CLAIMS

Claims rejected:	Claims 18-20
Claims allowed:	none
Claims canceled:	Claims 21-22
Claims withdrawn:	none
Claims on Appeal:	Claims 18-20 (A copy of the claims on appeal, as amended, can be found in the attached Appendix).

(4) STATUS OF AMENDMENTS AFTER FINAL

The Amendment after Final Rejection under 37 C.F.R. §1.116 filed 31 March 2003 has been entered for purposes of this appeal. See the Advisory Action, mailed 17 April 2003, indicating the Amendment would be entered upon filing of an appeal.

(5) SUMMARY OF THE INVENTION

Appellants' invention is directed to isolated polynucleotides encoding polypeptides identified as a novel human pyrophosphatase (HPYP), and to a method of detecting those polynucleotides in a sample.

Nucleic acids encoding HPYP were first identified in Incyte Clone 768320 from the lung tissue cDNA library LUNGNOTO4 through a computer-generated search for amino acid sequence alignments. HPYP is 289 amino acids in length and shares both chemical and structural homology with the partial sequence of a human pyrophosphatase (GI 727225; SEQ ID NO:3), a bovine

pyrophosphatase (GI 585322, SEQ ID NO:4) and a yeast pyrophosphatase (GI 4199; SEQ ID NO:5). In particular, HPYP shares 77% identity with the partial human pyrophosphatase sequence (SEQ ID NO:3) over the length of that molecule. The bovine and yeast pyrophosphatases each share 96% and 37% identity with HPYP, respectively. Despite the wide variation in overall sequence identity between these four molecules, all of them contain the seventeen amino acid residues previously identified as being important for pyrophosphatase activity (Lahti, R et al. (1990) Biochim Biophys Acta 1038:338-345). In particular, the sequence, DEGETDWK, beginning at amino acid residue D(148), is identical for all four molecules. As illustrated by Figures 3 and 4 of the Specification, HPYP and bovine pyrophosphatase have rather similar hydrophobicity plots. Northern analysis (Figure 5 of the Specification) shows the expression of this sequence in various libraries, at least 43% of which are immortalized or cancerous and at least 24% of which involve immune response. Of particular note is the expression in thyroid tissue, colon tumor and rheumatoid arthritis. Specification at page 10, line 24 to page 10, line16.

The polynucleotides of the present invention are useful, for example, in providing new diagnostic or therapeutic compositions useful in the treatment of diseases and conditions associated with uncontrolled cell signaling and cell proliferation such as inflammatory diseases and cancer.

(6) ISSUE

Issue 1. Whether the Specification as filed provides sufficient disclosure to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph as to a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1.

(7) GROUPING OF THE CLAIMS

As to the single issue on appeal, all of the claims on appeal are grouped together.

(8) APPELLANTS' ARGUMENTS

Issue 1. **The rejection of Claims 18-20 under 35 U.S.C. § 112, first paragraph, for**

alleged lack of written description is improper as the claimed subject matter is adequately described in the Specification.

Claim 19, with dependent claims 18 and 20, stand rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description.

In particular, the Examiner asserts,

> "With regard to a naturally-occurring human polynucleotide sequence variant, there is no description of any mutational site that exists [sic] in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any allele including strictly neutral alleles. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. Thus the claimed genus is extremely variable with the potential to encode proteins with widely variant functions. The common attributes of the genus are not described. Therefore, one of skill in the art would not conclude that the applicant was in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims. Therefore, a naturally-occurring DNA encoding a polypeptide comprising a sequence having 90% identity to SEQ ID NO:1 lacks [sic] sufficient written description needed to practice the invention of claims 18-20." (Final Office Action of 31 December 2002, Paper No. 29, pages 3-4).

This rejection is respectfully traversed.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the

> specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]
>
> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., ***complete or partial structure***, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] ***If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.***[46] [emphasis added]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

1. The specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1

The subject matter encompassed by claims 18-20 is either disclosed by the specification or is conventional or well known to one skilled in the art.

Independent claim 19 in relevant part recites:

"An isolated polylnucleotide selected from the group consisting of ... b) a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1..."

Appellants respectfully assert that the disclosure in the Specification as filed is more than sufficient to satisfy the written description requirement of as to the claimed subject matter. In particular, the structures of SEQ ID NO:1 and SEQ ID NO:2 are specifically disclosed in the application (see, for example, Figures 1A-B, sequence listing, pages 47-49). Given the genetic code and SEQ ID NO:1, all possible polynucleotide sequences encoding SEQ ID NO:1 are therefore described. Variants of SEQ ID NO:2 which encode SEQ ID NO:1 are also explicitly described, for example, at page 11, line 26 through page 12, line 13.

Variants of the amino acid sequence of SEQ ID NO:1 are also described. In particular, the preferred, more preferred, and most preferred SEQ ID NO:1 variants (i.e., those having 80%, 90%, and 95% amino acid sequence similarity to SEQ ID NO:1) are described, for example, at page 11, lines 17-20. Finally, polynucleotide sequence variants which encode 90% homologs of SEQ ID NO:1 are described, for example, at page 12, lines 20-24, and at page 13, lines 7-14. The specification also describes (e.g., page 45, line 26 through page 46, line 18) how to use BLAST to determine whether a given sequence falls within the "at least 90% polypeptide sequence identity" scope.

The present application also describes how to identify, or make, the claimed polynucleotides. Incyte clones in which the nucleic acids encoding the human HPYP protein were first identified and libraries from which those clones were isolated are described, for example, at page 10, lines 24-29 of the Specification. Chemical and structural features of HPYP are described, for example, on page 16, lines 10-18.

Furthermore, claim 19, recites not only that the polynucleotide "variants" encoding an amino acid having at least 90% sequence identity to SEQ ID NO:1, but that they are also "***a naturally-occurring polynucleotide sequence variant***." Through the process of natural selection, nature will have determined the appropriate polynucleotide sequences. Given the information provided by SEQ ID NO:1 (the amino acid sequence of HPYP) and SEQ ID NO:2 (the polynucleotide sequence encoding HPYP), one of skill in the art would be able to routinely obtain "a naturally occurring

polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1..." as recited in claim 19. For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the specification of the instant application. See, *e.g.*, Example V at pages 41-43; and Example VI at p. 43. Thus, one skilled in the art need not make and test vast numbers of polynucleotide sequences that are based on the amino acid sequence of SEQ ID NO:1. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature.

The Examiner also asserts that,

> "[n]o other naturally-occurring human polynucleotides encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 are known in the art." Final Office Action page 5. and
>
> "Applicants argue that there are "at least 3 naturally occurring human polynucleotides [that] encode an amino acid sequence (g6563256, g5931602, and g4960208) that are 100% identical to the sequence of SEQ ID NO:1. This is not found persuasive because all three sequences became publicly available after the effective filing date of the instant application of 10/31/96. Furthermore, the sequence that is 100% identical to another sequence is the same sequence not a variant thereof." Advisory Action page 2.

Applicants respectfully disagree with the Examiner's remark that "[n]o other naturally-occurring human polynucleotides encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 are known in the art" because Applicants understood the statement as meaning there are no other naturally-occurring human polynucleotides encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 known in the art ***(namely, both prior and post the filing date of the instant application)***. Thus, Applicants provided 3 examples of human polynucleotides that are at least 90% identical to SEQ ID NO:1. Applicants have also found a sequence (g4583153) which is 99% and thus a variant of SEQ ID NO:1 (Exhibit A).

Therefore, given SEQ ID NO:1 and SEQ ID NO:2, one of ordinary skill in the art would

recognize that Appellants were in possession of the claimed invention, i.e., naturally-occurring polynucleotide variants encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1, as of the time of filing. Accordingly, the Specification provides an adequate written description of the recited polynucleotide sequences.

2. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a

vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

In the *Fiers* case, the Revel party argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides in terms of chemical structure, rather than on functional characteristics. For example, the "variant language" of claim 19 recites chemical structure to define the claimed genus:

> 19. An isolated polynucleotide selected from the group consisting of ... b) a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1...

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO: 1. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides recited by the claims. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polynucleotides. The polynucleotides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a

written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

B. The present claims do not define a genus which is highly variant

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <40% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to polynucleotides encoding novel human inorganic pyrophosphatases related to the amino acid sequence of SEQ ID NO:1. In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as human pyrophosphatase proteins and which have as little as 40% identity over at least 70 residues to SEQ ID NO:1. The "variant language" of the present claims recites, for example, "a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 (note that SEQ ID NO:1 has 289 amino acid residues). This variation is far less than that of all potential human pyrophosphatase proteins related to SEQ ID NO:1, i.e., those human pyrophosphatase proteins having as little as 40% identity over at least 70 residues to SEQ ID NO:1.

Therefore, as discussed above, the present claims encompass naturally-occurring polynucleotides encoding amino acid sequences having at least 90% sequence identity to the sequence of SEQ ID NO:1.

C. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of October 31, 1996. Much has happened in the development of recombinant DNA technology in the 18 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1 and SEQ ID NO:2, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

2. The Examiner has attempted to apply a standard for written description different from that which is required by law

The Examiner has alleged that claims 18-20 do not comply with the requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph because:

> "Applicants specially disclose only a single representative of the entire claimed genus, SEQ ID NO:2. Said claimed genus is extremely variable with the potential to encode proteins with widely variant functions. The correlation between structure and function common to the members of the genus is not described. It is not conventional in the art to predict as to how the structure of one naturally-occurring sequence is representative of unknown sequences. Furthermore, no other naturally-occurring human polynucleotides encoding an amino acid sequence having at least 90% sequence

identity to the sequence of SEQ ID NO:1 are known in the art." Final Office Action page 5.

Applicants submit that neither the written description requirement of 35 U.S.C. 112, first paragraph nor any case law that interprets the statute has ever set forth such a standard. Furthermore, case law in the area of the written description requirement of 35 U.S.C. 112, first paragraph is clear with regard to the details considered sufficient to describe a claimed genus:

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

The specification sets forth a description of the claimed polynucleotide variants using "other appropriate language" as indicated above in connection with the remarks regarding "naturally-occurring polynucleotide variants encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1." The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:1 at, for example, Figures 1A-B. The specification provides a means of identifying naturally occurring functional variants having 90% sequence identity with SEQ ID NO:1 at, for example, page 10, lines 24-29. Applicants therefore submit that the "genus is sufficiently identified in [the instant] application by 'other appropriate language'" as stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960). Furthermore, Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, claims

18-20 meet the statutory requirements for written description under 35 U.S.C. 112, first paragraph.

3. The Examiner did not follow the guidance of the MPEP regarding written description requirements for nucleic acid and amino acid sequences

The MPEP addresses the issue of adequate written description of nucleic acid and amino acid sequences in the following manner:

> in the molecular biology arts, ***if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence***. Since the genetic code is widely known, ***a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence...*** [emphasis added] MPEP 2163 II A.3. (a) ii) (page 2100-165).

Applicants have disclosed the amino acid sequence of the SEQ ID NO:1 polypeptide in the present Specification (see, for example, Figures 1A-B and pages 47-48 of the Sequence Listing). Further, they have adequately disclosed 90% sequence variant of SEQ ID NO:1, as described above. Accordingly, the Examiner must accept that "applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence" as directed by MPEP 2163 II A.3. (a) ii).

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1 and SEQ ID NO:2. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides defined by the present claims is adequately described, as evidenced by Brenner et al and consideration of the claims of the '740 patent involved in *Lilly*.

Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

Moreover, to the extent the above rejections were based on the Revised Interim and final Examination Guidelines and Training Materials, those portions of the Guidelines and Training Materials that form the basis for the rejections should be determined to be inconsistent with the law.

Due to the urgency of this matter, including its economic and public health implications, an expedited review of this appeal is earnestly solicited.

(9) CONCLUSION

The written description rejection with respect to the claimed "variants" should be reversed, based on at least the arguments presented above.

If the USPTO determines that any additional fees are due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

This brief is enclosed in triplicate

Respectfully submitted,

INCYTE CORPORATION

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APPENDIX - CLAIMS ON APPEAL

18. (Original) The method of claim 20, wherein before hybridization, the target polynucleotide is amplified by the polymerase chain reaction.

19. (Original) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide sequence of SEQ ID NO:2,

b) a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1, and

c) a polynucleotide sequence complementary to a) or b).

20. (Currently Amended) A method of detecting a target polynucleotide in a sample, said target polynucleotide having the sequence of a polynucleotide of claim 19, comprising hybridizing the sample with a probe comprising at least 60 contiguous nucleotides of a sequence completely complementary to SEQ ID NO:2, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide, and detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.